DOCKET NO: 253871US0PCT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF	:
THOMAS BECKERT, ET AL.	: EXAMINER: SHEIKH, H.N.
SERIAL NO: 10/501,236	:
FILED: JULY 12, 2004	: GROUP ART UNIT: 1615

FOR: PHARMACEUTICAL FORMULATION FOR THE ACTIVE INGREDIENT BUDESONIDE

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

REPLY BRIEF

This Reply Brief is timely filed on August 11, 2010, with no extensions of time. This Reply Brief responds to erroneous findings and conclusions throughout the Examiner's Answer dated June 11, 2010.

Applicant notes, with appreciation, the statements at page 2, paragraph (3), and page 3, paragraph (6), of the Examiner's Answer (Ans.), that the final rejection of separately argued Claim 3 has been "withdrawn" and that "Claim 3 is allowable."

STATUS OF CLAIMS

Claims 1, 2, 4-8, and 10-12 stand twice REJECTED under 35 U.S.C. § 103.

Claim 3 is now ALLOWABLE.

Claims 1, 2, 4-8, and 10-12 are APPEALED

Claim 17 stands WITHDRAWN (non-elected invention).

Claims 9 and 13-16 are CANCELED.

The final rejection of Claims 1, 2, 4-8, and 10-12 under 35 U.S.C. § 103(a) over Beckert (WO 01/68058, published September 20, 2001) is APPEALED.

STATUS OF AMENDMENTS

No amendment to Claims 1, 2, 4-8, and 10-12 on appeal have been filed or entered subsequent to the final rejection in the Office Action dated August 19, 2009.

GROUNDS OF REJECTION TO BE REVIEWED

1. The final rejection of Claims 1, 2, 5-8, 10, and 12 under 35 U.S.C. § 103 as unpatentable in view of Beckert (WO 01/68058, published September 20, 2001). Dependent Claims 2, 5-8, 10, and 12 stand or fall together with independent Claim 1.

2. The final rejection of Claim 4 under 35 U.S.C. § 103 as unpatentable in view of Beckert is separately argued from the rejection of Claim 1.

3. The final rejection of Claim 11 under 35 U.S.C. § 103 as unpatentable in view of Beckert is separately argued from the rejection of Claim 1.

ARGUMENT

1. Rejections of Claims 1, 2, 5-8, 10, and 12 under 35 U.S.C. 103 over Beckert

The Examiner maintains the final rejection of Claims 1, 2, 4-8, 10, and 12 under 35 U.S.C. § 103 as obvious to a person having ordinary skill in the art at the time the invention was made in view of Beckert's prior disclosure despite Beckert's many deficiencies. For example:

The Examiner's Answer acknowledges that Becker'454 does not recognize any of the solubility and release problems peculiar to budesonide, the only active ingredient required in Applicant's claimed pharmaceutical formulation (Ans., p. 5, 2nd full ¶). Nevertheless, the Examiner states that it is not necessary for a conclusion of obviousness that the applied prior art recognizes either the specific problems recognized or advantages disclosed in Applicant's Specification (Ans., p. 5, 2nd full ¶). While the Examiner's statement is supported by precedent, that precedent does not stand for the proposition that a conclusion of obviousness is sustainable over prior art which, as here, does not provide any other reason for making and using, or desire to make and use, the claimed pharmaceutical formulation.

The Examiner further acknowledges that "Beckert does not teach the instant rate of release of budesonide of more than 80% after 30 minutes" (Ans, pp. 6-7, bridging ¶). To the contrary, Beckert's "multilayer pharmaceutical product releases less than 5% of the active pharmaceutical ingredient during the first 2 hours of a USP release test and from 30 to 80% of the active pharmaceutical ingredient 8 hours after the start of the test" (Beckert'454, Claim 1). The Board should also note the results of Beckert's release test at pH 7.5 (Beckert'454, col. 11, l. 21, to col. 12, l. 2), which are shown in its Fig 2. Beckert's release rate is substantially different than the release rate required for the pharmaceutical preparation Applicant claims.

The different release rates should not be surprising, because Applicant's inner layer is an "inner layer with the active ingredient budesonide bound in a binder . . . wherein the binder is a polymer or copolymer with acidic groups" (Claims Appendix, Claim 1 a) and final "wherein" clause). The inner layer of Applicant's claimed pharmaceutical formulation corresponds to the "core" of the inventive multilayer pharmaceutical product claimed in Beckert'454 (Beckert'454, Claim 1). The "inner layer coating" of the multilayer pharmaceutical product of Claim 1 of Beckert'454 corresponds to the "intermediate layer with a polymeric coating" of Applicant's appealed Claim 1 (Claims Appendix, Claim 1). Nevertheless, the Examiner finds (Ans., p. 7):

(1) "Beckert'454 explicitly teaches a polymer or copolymer with acidic groups"; and

(2) "Beckert meets Applicant's claimed requirement for a 'binder that is a polymer or copolymer with acidic groups' as recited in instant Claim 1."

A significant error in the Examiner's findings is the fact that the active ingredient, e.g., budesonide, present in the "core" of the multilayer pharmaceutical products disclosed and claimed in Beckert'454 is not "bound in a binder . . . wherein the binder is a polymer or copolymer with acidic groups" as Applicant's claims require (Claims Appendix, Claim 1; emphasis added). To the contrary, any polymers or copolymers with acidic groups disclosed in Beckert'454 form either the "inner coating of a copolymer" or the "outer coating of a copolymer" for the active ingredient in the core of the multilayer pharmaceutical product disclosed and claimed in Beckert'454, which inner coating and outer coating respectively correspond to the "intermediate layer with polymeric coating" or the "outer envelope . . . or an outer layer with a coating" in Applicant's claimed pharmaceutical formulation.

Unfazed by what appears on its face to be substantially different structures and rates of release for the products disclosed and claimed in Beckert'454 and the formulations of Applicant's appealed Claim 1, the Examiner erroneously found that, because Beckert'454 teaches a "polymer or copolymer with acidic groups" may form either an inner layer or outer layer which coats the core of the multilayer product Beckert'454 discloses and claims, the budesonide in the core of the product disclosed and claimed in Beckert'454 would necessarily be "bound in a binder . . . wherein the binder is a

polymer or copolymer with acidic groups" as Applicant's claims require. Even though that definition of Applicant's inner layer is entirely inconsistent with the active ingredient-free inner and outer coatings described in Beckert'454, the proof that the Examiner's interpretation of Applicant's claim language is inconsistent with the Specification and erroneous is the Examiner's acknowledgement that "Beckert does not teach the instant rate of release of bundesonide of more than 80% after 30 minutes" (Ans, pp. 6-7, bridging ¶). The release rates required for Applicant's claimed formulation are completely different from the release rates required for the multilayer product Beckert'454 discloses and claims.

Nevertheless, because the Examiner finds structural similarities between the prior art multilayer products and the multilayer formulation Applicant claims, the Examiner erroneously finds that the solubility and release problems associated with the use of budesonide as the active ingredient would be inherently be the same or substantially the same (Ans., p. 8). Though contrary to the evidence of record, even if that finding is presumed correct, persons having ordinary skill in the art would not have been led by any unrecognized solubility and release problems inherent in the use of budesonide to drastically modify the release rates Beckert'454 specifically requires for its multilayer product. The normal desire of scientists or artisans is to improve upon what is generally known. Prior knowledge is the motivation to improve. *In re*

Peterson, 315 F.3d 1325, 1330 (Fed. Cir. 2003). Persons having ordinary skill in the art are not moved to correct unrecognized problems.

Not finding any structural differences whatsoever between the prior art multilayer products and Applicant's claimed formulation, the Examiner's Answer nevertheless generally finds that "Beckert clearly teaches a polymer or copolymer with acidic groups" somewhere in its multilayer product and therefore argues that a disclosure a polymer or copolymer with acidic groups anywhere in the multilayer product taught by Beckert'454 is sufficient evidence to establish the obviousness of the specific pharmaceutical formulation Applicant claims. While the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), recognized that a conclusion of obviousness under 35 U.S.C. § 103 at times may be based on "obvious-to-try" rationale and/or invitations to experiment with reasonable expectation of success, that learned Court never suggested that it would have been obvious for persons having ordinary skill in the art to find a teaching of polymers or copolymers with acidic groups somewhere in a multilayer structure and reposition those polymers or copolymers anywhere else in the same multilayer structure to achieve an entirely different result, i.e., a significantly different drug release rate.

Nevertheless, the Examiner's conclusion of obviousness in this case takes that fiction a step further. The Examiner states (Ans., p. 10, 1st full ¶):

> [T]he determination of effective rates of release or profiles is within the level of the skilled artisan, obtained via routine optimization process. The Beckert reference suggests and teaches use of a polymer or copolymer with acidic groups, as presently claimed.

The Examiner appears to conclude that persons having ordinary skill in the art with (1) no prior knowledge of the solubility and release problems peculiar to budesonide release in the intestines, (2) no teaching in Beckert'454 to bind core budesonide in a binder of polymer or copolymer with acidic groups, and (3) specific instructions in Beckert'454 to release from 30 to 80% of the active ingredient 8 hours at pH 7.0-7.5, would have been led by the teaching of Beckert'454 as a whole to optimize the budesonide release rate of its multilayer product by adding a polymer or copolymer with acidic groups to bind the budesonide in the core of the multilayer product taught by Beckert'454 in order to release budesonide in the intestines at a rate significantly faster than any rate recommended by Beckert'454 without undue experimentation and with reasonable expectation of success. Applicant suggests that persons having ordinary skill in the art using basic common sense and applying all the prior knowledge in the art reasonably would not have been led to the product defined by Applicant's appealed claims.

While persons having ordinary skill in the art have much knowledge and many skills, they are not the technological soothsayers the Examiner presents to this Board to accept. Rather, they are ordinary artisans.

2. Rejection of Claim 4 under 35 U.S.C. § 103 in view of Beckert

The Examiner's explanation why dependent Claim 4 wherein Applicant's intermediate layer is a (meth)acrylate copolymer which comprises 40 to 100% by weight free-radical polymerized units of C_1- to C_4-alkyl esters of acrylic or methacrylic acid and no or up to 60% by weight (meth)acrylate monomers with an anionic group in the alkyl radical would have been prima facie obvious in view of Beckert's disclosure of an intermediate layer comprising a (meth)acrylate copolymer which comprises 85 to 98% by weight free-radical polymerized C_1- to C_4-alkyl esters of acrylic or methacrylic acid and 15 to 2% by weight (meth)acrylate monomers with a cationic quaternary ammonium group in the alkyl radical (Beckert '454, col. 4, l. 53, to col. 5, l. 41) is confusing and difficult to understand (Ans., pp. 10-11, bridging ¶). What is well understood is the fact that that cationic quaternary ammonium groups are not anionic acidic groups and the percentages are different. Why the open nature of the Claim 4 is said to support the Examiner's rejection is a mystery.

What makes the Examiner's conclusion even more confusing is the fact that the Examiner appears to suggest that the polymers or copolymers having acidic groups disclosed in Beckert'454 for use as the outer layer coating may be liberally and interchangeably used also to form the binder in the inner layer, the coating of the intermediate layer, and/or the coating of the outer layer of its multilayer product without any significant effect on the release rate of the

budesonide from the inner layer or core. Beckert'454 teaching is broad, but not that broad.

Beckert '454 does not teach or reasonably suggest that its inner layer, i.e., the intermediate layer of Applicant's claimed multilayer formulation, should or may be a polymer or copolymer with anionic acidic groups or a polymer or a (meth)acrylate copolymer free of quaternary ammonium groups. While Beckert's outer layer may indeed be a polymer or copolymer with acidic groups, Beckert '454 does not invite persons having ordinary skill in the art to freely replace the inner layer with the outer layer for unspecified purposes. Obviousness is not an open invitation to experiment without any direction. The only direction to make and use the invention of Applicant's Claim 4 in this case is Applicant's own disclosure.

3. Rejection of Claim 11 under 35 U.S.C. § 103 in view of Beckert

In support of the rejection of Applicant's separately argued Claim 11, the Examiner states (Ans., p. 12, 1st full ¶; emphasis added):

> The Beckert reference is vividly suggestive of multiparticulate pellets or tablets compressed from pellets or tablets packed into capsules (see Claim 8 of Beckert) containing active agents such as budisonide.

Applicant can only assume that there is some heretofore unrecognized level of disclosure called "vividly suggestive" which would have suggested the pharmaceutical formulation defined by Applicant's Claim 11 without any express teaching, suggestion, motivation, or incentive to do so. This assumption is based on the fact that Beckert'454 does not provide persons having ordinary

skill in the art with any express teaching, suggestion, motivation, or incentive to make and use the product of Applicant's Claim 11. It is axiomatic in patent law that no amount of conclusory statements of arguments can replace a lack of objective evidence in support thereof. *In re De Blauwe*, 736 F.2d 699, 705 (Fed. Cir. 1984); *In re Lindner*, 457 F.2d 506, 508 (CCPA 1972).

CONCLUSION

For the reasons stated herein:

1. The rejections of Claims 1, 2, 5-8, 10. and 12 under 35 U.S.C. § 103 as unpatentable over Beckert should be REVERSED.

2. The rejection of Claim 4 under 35 U.S.C. § 103 as unpatentable over Beckert should be REVERSED.

3. The rejection of Claim 11 under 35 U.S.C. § 103 as unpatentable over Beckert should be REVERSED.

Respectfully submitted,

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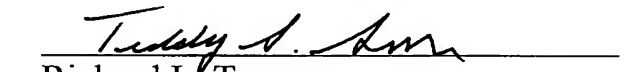

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